Epigenetics 8:12, 1247–1248; December 2013; © 2013 Landes Bioscience

In this issue of *Epigenetics*

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Regulation of Histone Modifications: Dual Functions for Spt6 pp. 1249–53

In order to maintain a specific chromatin state, modified histones must remain attached to template DNA during transcription. In fact, RNA polymerase II can transcribe the nucleosome template without changing nucleosome positioning. Recently, Spt6, a highly conserved polymerase-associated histone chaperone, was shown to prevent transcription-coupled loss of posttranslationally modified histone H3. Now, Kato et al. propose here that Spt6 has two fundamentally distinct functions in the regulation of histone modification: one is to act as a platform for histone modifiers and the other is as a molecular liaison between histone molecules and template DNA, preventing cotranscriptional dissociation of preexisting histones so that locus-specific modifications are maintained.

Epigenetic Differences between Human Cancer and Mouse Models pp. 1254–60

Primary human cancers show extensive cancer-specific CpG island DNA hypermethylation in critical developmental pathways. Diede et al. now studied whether genetically engineered mouse models (GEMMs) of different cancers show comparable epigenetic changes. In contrast to human samples, very few loci with cancer-specific DNA hypermethylation were detected in mouse models and, in almost all cases, the degree of methylation was relatively modest compared with the dense hypermethylation in the human cancers. These findings provide an opportunity to both better understand the mechanism of aberrant DNA methylation in human cancer and construct better GEMMs for therapy development.

A Putative Epigenetic Biomarker for Bacterial Sepsis pp. 1261–7

Diagnosis of bacterial sepsis in preterm neonates can be difficult when using serum markers that rely on physiological changes because these changes may not necessarily be the result of bacterial infections alone. Tendl et al. identified specific DNA methylation patterns of the promoter region of the *CALCA* gene associated with different types of bacterial preterm sepsis, suggesting its potential use as epigenetic biomarker.

Human and Mouse ZFP57 Proteins are Functionally Interchangeable pp. 1268–79

ZFP57 is a master regulator in genomic imprinting. Loss of ZFP57 causes loss of DNA methylation imprint at multiple imprinted regions in mouse embryos, as well as in embryonic stem cells. Mouse and human *Zfp57* genes are located in the same syntenic block. However, mouse and human ZFP57 proteins only display about 50% sequence identity. Takikawa et al. now report that mouse and human ZFP57 proteins are functionally interchangeable and suggest that mouse and human ZFP57 are orthologs despite relatively low sequence identity.

EZH2 and the Silencing of HOX Genes pp. 1280–8

HOX genes are preferentially methylated in mantle cell lymphoma (MCL) compared with chronic lymphocytic leukemia (CLL), despite these genes not being expressed in either entity. Since the chromatin modifier EZH2 has been shown to regulate HOX gene expression, and EZH2 is overexpressed in MCL, Kanduri et al. studied whether overexpression of EZH2 was involved in HOX genes regulation in MCL. The authors showed that hypermethylation of HOX genes in MCL resulted from EZH2 overexpression and subsequent recruitment of the DNA methylation machinery onto HOX gene promoters. These observations implicate EZH2 in the long-term silencing of HOX genes in MCL.

ABCA1 DNA Methylation and Maternal Metabolic Status pp. 1289–1302

The in utero environment is associated with epigenetic changes in the offspring and also with a lifelong susceptibility to cardiovascular disease (CVD). Now, Houde et al. assessed the associations between the maternal metabolic profile and *ABCA1* DNA methylation levels (previously associated with CVD) in placenta and cord blood. The authors report that *ABCA1* DNA methylation levels (and mRNA levels) are variable on both sides of the placenta (maternal and fetal) and conclude that these variations contribute to an optimal materno-fetal cholesterol transfer, which may also potentially trigger the long-term susceptibility of the newborn to dyslipidemia and CVD.

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Submitted: 11/14/2013; Accepted: 11/14/2013
http://dx.doi.org/10.4161/epi.27247

Enhancer Transcribed RNAs pp. 1303–20

A subset of enhancers are occupied by RNA polymerase II and transcribed to produce long non-coding RNAs termed eRNAs. Pulakanti et al. have now investigated the association between eRNA productivity and various chromatin marks and transcriptional regulators in mouse embryonic stem cells (ESCs). The authors found that that eRNA-producing enhancers exhibited elevated levels of the active mark H3K27Ac, decreased DNA methylation, and enrichment for the DNA hydroxylase Tet1.

Epigenetics of Maternal Mood Disorder and Newborn Neurobehavior pp. 1321–9

Exposure to maternal mood disorder in utero may program infant neurobehavior via DNA methylation of two placental genes (*NR3C1* and *11*β*-HSD-2*) that have been implicated in perturbations of the hypothalamic pituitary adrenocortical axis. Conradt et al. tested the relations among prenatal exposure to maternal depression or anxiety, methylation of exon 1F of *NR3C1* and *11*β*-HSD-2*, and newborn neurobehavior. Their results support the fetal programming hypothesis and suggest that fetal adjustments to cues from the intrauterine environment, in this case an increased exposure to maternal cortisol, may lead to poor neurodevelopmental outcomes.

Epigenetic Regulation of Anti-Angiogenesis Factors: From Tumor Dormancy to Active Growth pp. 1330–46

The initiation of angiogenesis can mark the transition from tumor dormancy to active growth and recurrence. Lyu et al. tested the expression level of angiogenesis factors and their epigenetic regulation using two inducible ovarian cancer cell lines. The authors found that the expression of the anti-angiogenic genes *TIMP3* and *CDH1* is elevated during dormancy and is reduced during the transition to active growth by changes in DNA methylation and histone modification.

Epigenetic Inactivation of *VHL* in Neuroendocrine Tumors pp. 1347–54

Pheochromocytoma (PCC) and abdominal paraganglioma (PGL) are neuroendocrine tumors that present with clinical symptoms related to increased catecholamine levels. About a third of the cases are associated with constitutional mutations in predisposing genes, of which some may also be somatically mutated in sporadic cases. Andreasson et al. assessed the methylation density and gene expression levels of 11 PCC/PGL disease genes in tumors and in normal adrenal references. The authors show that the *VHL* gene promoter has increased methylation compared with normal adrenals in approximately 75% of PCCs and PGLs investigated, highlighting the role of *VHL* in the development of these tumors.

Recurrent Patterns of DNA Methylation in Different Cancers pp. 1355–72

In a comprehensive study, Sánchez-Vega et al. identified 12 loci that are differentially methylated in serous ovarian cancers, in endometrioid ovarian and endometrial cancers, and in normal control samples. The strongest signal showed hypermethylation in tumors at a CpG island within the *ZNF154* promoter. Hypermethylation of this locus is recurrent across solid human epithelial tumor samples for 15 of 16 distinct cancer types. In addition, the authors also identified recurrent hypomethylation in two genomic regions associated with *CASP8* and *VHL*. These three genes exhibit significant negative correlation between methylation and gene expression across many cancer types, as well as patterns of DNaseI hypersensitivity and histone marks that reflect different chromatin accessibility in cancer vs. normal cell lines.

Epigenetic Regulation of *DACH1* in Colorectal Cancer pp. 1373–83

Loss of DACH1 expression was found in breast, prostate, and endometrial cancer. Yan et al. have analyzed the regulation and function of DACH1 in colorectal cancer. Their results suggest that DACH1 expression is regulated by promoter region hypermethylation in CRC and that *DACH1* methylation was associated with late tumor stage, poor differentiation, and lymph node metastasis. Therefore, methylation of *DACH1* may serve as detective and prognostic marker in CRC.